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Glycemic Outcomes of Oral Hypoglycemics Versus GLP-1 Receptor Agonists in Type 2 Diabetes: A Comparative Clinical Study

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is one of the most significant health concerns around the world, especially in South Asian communities, where the escalating burden of obesity and sedentary lifestyles has intensified the disease. Although oral hypoglycemic agents (OHAs) remain first-line treatment, glucagon-like peptide-1 (GLP-1) receptor agonists have become an effective alternative since they have a glucose-dependent insulinotropic effect, reduce weight, and have fewer adverse effects, particularly hypoglycemia. There is limited comparison of clinical evidence of local settings, however.

Objectives: To evaluate the efficacy of OHAs and GLP-1 receptor agonists in enhancing glycemic regulation in adults with T2DM.

Methods: A comparative clinical study was carried out in Shaikh Zayed Hospital, Lahore, between January 2024 and March 2025. Eighty adult participants with T2DM were recruited through consecutive sampling and separated into 2 equal groups: Group A was provided with regular OHAs and Group B was prescribed GLP-1 receptor agonists. Fasting blood sugar (FBS), random blood sugar (RBS), and HbA1c were measured at baseline and 6 months. Statistical software SPSS 26 version was utilized and p less than 0.05 was regarded to be significant.

Findings: Both groups experienced an improvement in glycemic parameters and the GLP-1 group had significantly more decreases in the HbA1c (1.8 vs. 1.0), FBS and RBS ($p < 0.01$). Also, the GLP-1 group obtained significant losses (3.4 kg) in weight, but the OHA did not. Hypoglycemia was more prevalent among users of OHA whereas gastrointestinal symptoms were a little bit more prevalent among users of GLP-1.

Conclusion: GLP-1 receptor agonists offer a benefit in glycemic control and weight loss over traditional OHAs and reduced hypoglycemic events. These agents are a good therapeutic alternative in the management of T2DM, particularly when the patient needs a better metabolism.

Keywords: Diabetes, Glycemia, GLP-1, Hypoglycemia, Obesity, Treatment, Incretins, Insulin, Metabolism

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INTRODUCTION

Diabetes Mellitus type 2 (T2DM) is a highly growing global chronic metabolic condition, whereby the body develops progressive insulin resistance, impaired pancreatic-cell functionality, and incurable hyperglycemia [1]. Recent estimates of the global population indicate that there are over 530 million adults with diabetes today, and that the number is bound to shoot up over the next 20 years, with the heaviest load likely to be experienced in the low- and middle-income countries, such as Pakistan. The further increase in obesity, sedentary living, urbanization, and bad eating patterns has also played a great role in the rising prevalence of T2DM among South Asians. The uncontrolled hyperglycemia over the long term is a significant stimulant of microvascular complications like retinopathy, nephropathy, and neuropathy, and

macrovascular diseases such as myocardial infarction and stroke. The resultant effects impose high financial and social cost on the health care systems, and thus effective glycemic control becomes a key concern in the management of diabetes [2,3].

Oral hypoglycemic agents (OHAs) have been considered the backbone of pharmacological interventions for T2DM for decades. Metformin, sulfonylureas, thiazolidinediones, and DPP-4 inhibitors are among the agents that are still heavily utilized in clinical practices because they are cheap, easy to administer, and have proven efficacy. Nevertheless, in spite of such advantages, OHAs possess significant drawbacks [4]. A significant number of patients will not receive optimal glycemic levels because of deteriorating 2-cell function, reduced response to treatment after a time span, or lack of compliance. Also, weight increase, hypoglycemia, especially in the case of sulfonylureas, and gastrointestinal problems are side effects that cause clinical issues and discontinuation of treatment in a large percentage of patients [5].

Over the recent years, glucagon-like peptide-1 (GLP-1) receptor agonists have become an eye-opener in the treatment of T2DM. These incretin-based agents replicate the endogenous GLP-1, which increases glucose-dependent insulin secretion, suppresses glucagon release, slows down gastric emptying, and increases satiety [6]. Discriminatory physiological processes not only enhance glycemic control but also result in positive weight loss, reduced hypoglycemic risk, and cardiovascular protection evidenced in high-risk patients. All these strengths have placed the GLP-1 agonists as a more appealing alternative or complement to traditional OHAs, especially in people with obesity, poor glycemic regulation, or well-established cardiometabolic risk factors [7].

Although there is increasing evidence on the clinical superiority of GLP-1 receptor agonists in the world, there is little real-world comparative data in the regional healthcare setting. The usage of traditional OHAs in local prescribing remains predominant in terms of cost, little awareness, and lack of access to more advanced therapeutic agents [8]. Knowledge of comparative treatment outcomes is thus needed to inform evidence-based practice and optimize clinical practice in high metabolic disease burden populations [9].

The purpose of this study is to make a direct comparison of the oral hypoglycemic agents and GLP-1 receptor agonists on the provision of improved glycemic outcomes in adults with T2DM. The study aims to produce clinically applicable information by assessing the variation of fasting blood glucose, random glucose level, HbA1c, weight loss, and adverse effects of treatment within a specific follow-up period that can guide the therapeutic decision-making and lead to improved metabolic control in diabetic patients [10].

MATERIALS AND METHODS

The study was a comparative clinical study that was carried out in the Department of Endocrinology, Shaikh Zayed Hospital, Lahore, Pakistan, and conducted over fifteen months between January 2024 and March 2025. Data collection commenced only after the Institutional Review Board of Shaikh Zayed Hospital granted ethical approval to the study (Ethical Approval Reference No.: SZH/IRB/2023-144). The members were educated about the protocol of the study, and written consent was signed as per the Declaration of Helsinki.

Eighty (80) adult patients diagnosed with Type 2 Diabetes Mellitus (T2DM) were recruited. The research employed a non-probability sampling, and the consecutive sampling technique was used. Each patient who approached the Endocrinology outpatient clinics during the period of the study and qualified as per the inclusion criteria was approached and recruited until the target population size was reached. This has been used to allow the inclusion of all the qualifying patients in their natural course of clinical work, which minimizes selection bias and provides real-world applicability [11].

They included the participants aged 30-65 years having a confirmed diagnosis of T2DM for at least one year and with inappropriate glycemic control, which was 7.5 to 10.5. The patients were also locked out where they had Type 1 diabetes, chronic kidney disease stage 3 or above, extreme liver disease, active malignancy, had undergone pancreatitis and thyroid medullary carcinoma, were pregnant or lactating, or had previously taken a GLP-1 receptor agonist. The patients who had low medication compliance, incomplete follow-ups, or unavailable laboratory data were not considered either [12].

After the screening of the eligibility, the participants were divided into two comparative groups according to their current treatment. Group A (n = 40) consisted of patients who used standard oral hypoglycemic agents (OHAs), including metformin, sulfonylureas, thiazolidinediones, and DPP-4 inhibitors, as either monotherapy or combination therapy depending on clinical indication. Group B (n=40) included those patients who were undergoing GLP-1 receptor agonist therapy (daily liraglutide or weekly semaglutide) and the dosage was gradually increased based on the recognized international clinical guidelines in order to achieve optimal tolerability [13].

A structured questionnaire was used to collect baseline demographic and clinical data such as age, gender, time of diabetes onset, weight, comorbidities, and medication history. At the baseline of the study, laboratory tests in the form of fasting blood sugar (FBS), random blood sugar (RBS), and glycated hemoglobin (HbA1c) were conducted. All the laboratory tests were performed in the central diagnostic laboratory of the Shaikh Zayed Hospital using standard equipment that is subjected to regular calibration and quality control [14].

Follow-up on participants was done after six months, which was one month. Medication compliance was evaluated during every visit, and adverse events (hypoglycemia, GIT, and injection-site reactions) were recorded. External confounding factors were prevented by recommending consistent lifestyle habits, consumption of diet, and exercise to patients. The FBS, RBS, HbA1c, and body weight were again re-assessed at the end of six months using the same standardized laboratory methods [15].

Statistical analysis and entry of data were done by the use of SPSS version 26. Continuous variables were given in the form of mean and standard deviation, whilst categorical variables were in the form of frequencies and percentages. The Shapiro-Wilk test was used to determine the normal data distribution. In case of within-group comparisons across time, paired t-tests were applied. The independent-sample t-tests were used to determine between-group differences. The statistical significance was taken to be a p-value of less than 0.05 [16].

RESULTS

The final analysis was done on 80 patients diagnosed with Type 2 Diabetes Mellitus, with 40 participants in each group. There was a similarity in the demographic profile and baseline characteristics of both groups. Group A (OHA group) had a gender balance of 22 males (55 percent) and 18 females (45 percent), and Group B (GLP-1 receptor agonist group) contained 20 males (50 percent) and 20 females (50 percent), and there was no significant difference between the two groups ($p > 0.05$). No statistically significant differences in parameters of baseline clinical such as age, fasting blood sugar (FBS), random blood sugar (RBS), and HbA1c also indicated sufficient comparability (Table 1).

After the six-month treatment, both groups reported improvement in their glycemic control, but the level of improvement varied significantly. The average change in the HbA1c level was 1.0 in Group A and 1.8 in Group B ($p < 0.001$), respectively (Table 1). In Group A, the change in FBS was negative, i.e., 164 +22mg/dL to 140 +20mg/dL, and in Group B, the change was greater, i.e., 162 +21mg/dL to 124 +18mg/dL ($p < 0.01$). In the same manner, RBS fell to 238±34mg/dl to 196±30mg/dl in the OHA and GLP-1 groups, respectively ($p<0.01$).

The difference between groups also existed in weight change. GLP-1 agonists resulted in a large mean weight loss of 3.4 ± 1.1 kg in patients, whilst in the OHA group, it was only 0.5 ± 0.4 kg ($p < 0.001$). This is consistent with already established appetite-suppressant and metabolic properties of GLP-1 receptor agonists.

The negative effects were different in the groups. Hypoglycemia was more prevalent in the OHA group of patients (6 patients; 15%), as opposed to only 2 patients (5%), in the GLP-1 group. On the contrary, gastrointestinal intolerance (nausea, bloating, mild vomiting) was more prevalent in the GLP-1 group (25%) than in the OHA group (10%). Group B reported mild injection site reactions in 3 patients (7.5), but the reactions were temporary and did not cause treatment discontinuation.

Altogether, the comparison indicates that GLP-1 receptor agonists resulted in much greater improvements in glycemic parameters, body weight reduction in a more effective way, and a reduction of hypoglycemic events than traditional oral agents that could impact the glucose level.

Table 1: Baseline and Post-Treatment Glycemic Characteristics of the Study Groups

Variable	Group A (OHA)	Group B (GLP-1 Agonists)	p-value
Gender (M/F)	22 / 18	20 / 20	>0.05
Baseline Age (years)	51.4 ± 8.2	52.1 ± 7.9	>0.05
Baseline HbA1c (%)	8.6 ± 0.6	8.7 ± 0.7	>0.05
HbA1c After 6 Months (%)	7.6 ± 0.5	6.9 ± 0.4	**<0.001**
Baseline FBS (mg/dL)	164 ± 22	162 ± 21	>0.05
FBS After 6 Months (mg/dL)	140 ± 20	124 ± 18	**<0.01**
Baseline RBS (mg/dL)	238 ± 34	240 ± 36	>0.05
RBS After 6 Months (mg/dL)	196 ± 30	178 ± 27	**<0.01**
Weight Change (kg)	−0.5 ± 0.4	−3.4 ± 1.1	**<0.001**

Table 2. Comparison of Adverse Effects Between Groups

Adverse Effect	Group A (OHA) n (%)	Group B (GLP-1 Agonists) n (%)	p-value
Hypoglycemia	6 (15%)	2 (5%)	<0.05
Gastrointestinal Symptoms	4 (10%)	10 (25%)	<0.05
Injection-Site Reactions		3 (7.5%)	
Non-Adherence	5 (12.5%)	3 (7.5%)	NS

Table 1 shows that although both groups experienced improvement, the GLP-1 group demonstrated significantly greater reductions in all glycemic parameters and weight.

Table 2 demonstrates that hypoglycemia occurred more frequently in the OHA group, while gastrointestinal intolerance and injection-site reactions were more common in the GLP-1 group.

The results of the research prove that there is a significant disparity in the results of treatment in patients who use oral hypoglycemic agents (OHAs) and those who were assigned to the treatment with GLP-1 receptor agonists. The two groups improved the glycemic parameters after six months, although the extent of improvement was

much more marked in patients who were under GLP-1 therapy.

The biggest result was a decrease in HbA1c, with a mean decrease being 1.8 in the GLP-1 group and 1.0 in the case of the OHA group. This higher decrease means that GLP-1 agonists present an enhanced and more regular enhancement in the long-term glycemic regulation. Likewise, the level of fasting and random blood sugar (FBS and RBS) was reduced in all groups, but the GLP-1 group reflected more significant changes again. All these results indicate the increased glucose-lowering activity of GLP-1 receptor agonists, which would be explained by their dual effects on insulin secretion and glucagon inhibition.

The weight change also distinguished between the two treatments. GLP-1 group patients reported an average weight loss of 3.4 kg, and the weight loss of the OHA group was insignificant (0.5 kg). This result is in line with the physiological action of GLP-1 agonists, which stimulates satiety, slows gastric emptying, and promote weight loss, which is a key therapeutic benefit in overweight or obese diabetic patients. The results also show that the traditional OHAs do not significantly improve and that, in some cases, they might only add weight.

Patterns of adverse events were added information. Hypoglycemia was higher in OHA users (15%), and it is not surprising because of the presence of sulfonylureas and other insulin-stimulating drugs in this group. On the contrary, the incidence of hypoglycemia was much lower, namely 5 percent, in GLP-1 receptor agonists, which is indicative of a glucose-dependent action. In the meantime, gastrointestinal symptoms (nausea and bloating) were more common in the GLP-1 group (25%), which is also known to be an expected class effect. These were symptoms, though, which were mild and temporary. A minor percentage of patients who used injectable GLP-1 agents reported injection-site reactions, still not severe enough to withdraw.

On the whole, it can be suggested that the study results interpretation shows that GLP-1 receptor agonists are superior to the traditional oral hypoglycemic agents in terms of glycemic control, weight loss, and a reduced number of adverse effects. All these benefits render GLP-1 agents a useful treatment choice, especially in patients who have to have better glycemic control, have other weight management benefits, or those at higher risk of hypoglycemia.

DISCUSSION

This was a comparative clinical trial that assessed the efficacy of oral hypoglycemic agents (OHAs) in comparison with the efficacy of the GLP-1 receptor agonists in terms of improving glycemic control in patients who experienced Type 2 Diabetes Mellitus (T2DM) [13]. These findings obviously show that GLP-1 receptor agonists had much better results in terms of glycemic control, weight regulation, and the risk of hypoglycemia compared to the results of conventional OHAs [14].

The larger reduction in the HbA1c of the GLP-1 group is consistent with the evidence at the global level of the strong glucose-lowering effect of this type of drug. The average change in HbA1c of 1.8 in the GLP-1 group is greater than the average change that comes with metformin or sulfonylureas, which would be between 0.8 and 1.2 [15]. This indicates that GLP-1 receptor agonists can potentially provide extra advantages to patients who have poor glycemic control, even with oral therapy. The higher increment in both fasting and random blood glucose of the GLP-1 group further substantiates the pharmacologic benefit of incretin-based therapy, which increases glucose-dependent insulin secretion and inhibits the inappropriate secretion of glucagon [16].

The secondary outcome was weight reduction in patients who take GLP-1 agonists. The average weight loss experienced in this paper was 3.4kg of weight relative to the insignificant weight decrease in the OHA group [17]. This has clinical significance because insulin resistance and cardiovascular morbidity in T2DM are major contributors to obesity. This has likely been due to the appetite-lowering and gastric-emptying effects of GLP-1 agonists, which are also in line with prior randomized trials showing the same. The neutrality or even weight gain with sulfonylureas and thiazolidinediones also adds to the therapeutic benefit of GLP-1-based regimens in overweight or obese patients [18].

The known pharmacological profiles of the two categories of treatments were in line with adverse effects. There was a greater prevalence of hypoglycemia among the OHA group, especially when using sulfonylureas, as the insulin-independent stimulation of β-cells occurred. Contrarily, GLP-1 receptor agonists demonstrated significantly reduced incidences of hypoglycemia, which is also indicative of their safety profile. Gastrointestinal symptoms were more frequently reported in GLP-1 users, but these were usually mild and short-lived. Injury-site reactions were only seen in some patients, but they did not affect the treatment adherence and tolerability [19,20].

This study supports the increasing trend to use GLP-1 receptor agonists in the current diabetes management guidelines, especially in obese patients with inadequate glycemic control or intolerance to oral medications. They also have other cardiovascular advantages, which were proven in the course of multiple large-scale clinical trials, making them even more valuable in terms of therapy [13,16].

Nevertheless, this research does not lack limitations. The non-probability consecutive technique of sampling can be a constraint to generalization. Although the six-month follow-up duration is adequate to provide initial glycemic evaluation, it might not give all the long-term results like weight loss sustainability, cardiovascular guarding, and drug adherence. Also, the cost and accessibility were not considered, which can affect the treatment choice in clinical practice, especially in populations with low and middle income [21,22].

Nevertheless, the study offers powerful comparative evidence based on a real-life Pakistani clinical setting and is of important value to endocrinologists and primary-care physicians working with T2DM in the local health care settings [23].

CONCLUSION

The GLP-1 receptor agonists demonstrated improved glycemic control, weight loss, which carries significance as well, and a lower incidence of hypoglycemia compared to the conventional oral hypoglycemic agents in Type 2 Diabetes Mellitus. The findings support the use of an GLP-1 agonist as one of the therapeutic interventions of favorable and safe efficacy, especially in patients with excess weight, poor glycemic response to OHAs, or increased risks of hypoglycemia. The addition of GLP-1 therapies to the disease management plan has the potential of improving both long-term and short-term metabolic outcomes of the patient and improving the overall patient care.

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Authors' Contributions:

I.H.: Study concept, design, data acquisition, and manuscript drafting.

T.S.: Methodology, statistical analysis, and critical review.

S.S.: Data collection, literature review, and initial drafting.

H.M.E.: Data management, analysis support, and proofreading.

M.H.N.: Literature search, referencing, and final editing.

Data Availability Statement: The data used in this study are available upon reasonable request from the corresponding author, subject to ethical and institutional guidelines.

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